PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Thomas P. Quinn and
Natalia G. Karasseva

Serial No.: 10/520,408

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For: Erb-2 RECEPTOR TARGETING PEPTIDE

Group Art Unit: 1643

Examiner: Anne L. Holleran

Atty. Dkt. No.: UVMO:023US

Confirmation No.: 2719

INVENTORS' DECLARATION UNDER 37 C.F.R. §1.132

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

We, the undersigned, do declare that:

1. I am a citizen of the Unites States and reside at 5700 Stanley Pitts Lane, Columbia, Missouri.

2. I currently hold the position of Professor of Biochemistry at the University of Missouri-Columbia. I have conducted research in the area of Biochemistry for the past 30 years. A copy of my *curriculum vitae* is attached.

3. I am collaborating with the inventors' laboratory to develop novel cancer imaging agents. We have used a radiolabeled KCCYSL peptide analog to image breast and prostate tumors in

mouse models of disease. A manuscript describing this work will be published by Clinical Cancer Research this month. In that publication, we report the modification of the peptide KCCYSL for tumor targeting by linking it to a radiometal chelator (DOTA) with a spacer peptide sequence (Gly-Ser-Gly) to yield DOTA-GSG-KCCYSL. The addition of the GSG linker peptide improves peptide binding of the erbB-2 receptor up-regulated on the tumor cells.

4. In a separate series of experiments, we have made MAP-4 and MAP-8 constructs of KCCYSL to improve its affinity. The MAP-4 and MAP-8 molecules contain 4 and 8 copies of GSG-KCCYSL linked via a lysine tree. Multiple copies of the KCCYSL linker via branched peptides showed much higher affinity for cancer cells than the single KCCYSL sequence. The KCYSL sequence has also been incorporated into hetero-MAP constructs, where a MAP contained two GSG-KCCYL sequences and two P30 TF antigen binding peptides linked together in one peptide. This allows us to target tumor antigens on the cell at the same time, improving specificity and affinity. We are currently synthesizing a single polypeptide with two copies of KCCYSL in it. The peptide has the sequence DOTA-GSG-KCCYSL-(GSG)3-KCCYSL. This bi-dentate molecule will be compared to the MAP constructs to determine which presentation yield the best binding affinity and in vivo pharmacokinetics.

5. In summary, we have used the KCCYSL sequence as a monomer, in complex homo- or hetero-MAP constructs with up to 8 copies, and in multiple representations in a single polypeptide. Clearly, these data demonstrate that this peptide sequence can be incorporated into larger peptides and even macromolecules and still retain its erbB-2 targeting properties.

6. I declare that all statements made herein of my own knowledge are true, and that all statements of my own belief are believed to be true, and further that these statements were made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under § 1001 of title 18 of the United States Code.

Date: 10/24/07

Susan L. Deutscher